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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Olson & Hierl LTD
20 North Wacker Drive
36th Floor
Chicago, IL 60606

EXAMINER	
SLOBODYANSKY, ELIZABETH	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 02/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/637,302	HOOD ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky, PhD	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5,6,14,15 and 41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,6, 14, 15 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 11, 2003 has been entered.

The AF amendment filed October 10, 2003 canceling claims 2, 7-13, 16-40 and 42-67 and amending claims 1, 3, 5, 6 and 41 has been entered.

Claims 1, 3, 5, 6, 14, 15 and 41 are pending.

Claim Objections

Claims 1 and 41 are objected to because of the following informalities: a semicolon is missing after "the group consisting of".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 41 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 41 has been amended to recite "at least about 0.1 weight percent of an active Raf protein" (emphasis added). While the specification has support for ""at least 0.1 weight percent" (page 36, line 1), the examiner is unable to locate adequate support in the specification for ""at least about 0.1 weight percent". Thus there is no indication that such limitation was within the scope of the invention as conceived by Applicants at the time the application was filed.

Accordingly, Applicants are required to cancel the new matter in the response to this Office Action.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 5, 6, 14, 15 and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, with dependent claims 3, 5, 6, 14, 15 and 41, recites "a protein having the amino acid sequence corresponding to residues 306 through 648 of SEQ ID NO:2" (emphasis added). It is unclear which proteins other than the 306-648 fragment of SEQ

ID NO:2 are encompassed by the claim rendering the metes and bounds of the claim unascertainable.

Claim 41 recites "at least about 0.1 weight percent of an active Raf protein" rendering the metes and bounds of the claim indefinite (emphasis added). The term "at least" means "no less than 0.1 percent" whereas "at least about" encompasses values below 0.1 as well.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 5, 6, 14, 15 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Freed et al. alone or in view of Przybyszewska et al.

Freed et al. (US Patent 5,597,719, form PTO-892 mailed July 15, 2003) teach human Raf protein of SEQ ID NO:2 that is 100% identical to SEQ ID NO:2 of the instant invention and its functional fragments (columns 1-4, line 15). Said fragments include C-terminal kinase domain 303-648 and raf-CAAX (Figure 4; column 6; column 16, lines 55-65; column 27, lines 5-29; column 31,lines 4-5). They teach expression of the full length Raf and its fragments in host cells (column 18). They further teach isolation of

Raf proteins by immunoprecipitation using a Raf specific antibody (column 14, lines 24-49).

Przybyszewska et al. teach that transfection of human urothelial cells (HCV-29) results in two-fold increase of said cells ability to stimulate angiogenesis *in vivo* (abstract, page 159, Table 1). They teach that "it could be expected that raf plays a critical role in the induction of angiogenesis" (page 160, last paragraph). The teachings of Przybyszewska et al. provide the motivation to make a pharmaceutical composition comprising a raf protein to be administered for stimulation of angiogenesis.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce c-Raf protein (SEQ ID NO:2) or its fragments by the expression in a host cell and isolating them therefrom using a specific antibody as taught by Freed et al. A buffer solution comprising an isolated c-Raf protein or its fragments represents a pharmaceutical composition (specification, page 35). The motivation to produce a buffer solution, i.e. a pharmaceutical composition comprising a Raf protein is provided by Freed et al. who teach its importance in various pathological conditions (columns 1-2). The teachings of Przybyszewska et al. provide the motivation to make a pharmaceutical composition comprising a raf protein to be administered for stimulation of angiogenesis. It would have been obvious to use a human Raf protein or its known active fragments taught by Freed et al. in said pharmaceutical composition. With regard to claim 41, it is customary to make a pharmaceutical composition comprising at least 0.1 weight percent of an active ingredient.

It would have been further obvious to one of ordinary skill in the art to produce an article of manufacture comprising a pharmaceutical composition comprising Raf protein of SEQ ID NO:2 or its fragments and fusions and an identifying label optionally containing instructions for use.

Statement of intended use in a pharmaceutical composition claim does not distinguish it over the prior art product, i.e. a pharmaceutical composition comprising Raf protein is the same product independent on its intended use.

Claims 1, 3, 6, 14,15 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kolch et al. alone or in view of Przybyszewska et al.

Kolch et al. teach the production of the full length and truncated versions of the human c-Raf-1 protein (page 1046). They suggest the use of said purified proteins the production of antisera, for example (page 1048, last paragraph).

The teachings of Przybyszewska et al. are outlined above.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce c-Raf protein or its fragments by the expression in a host cell and isolating them therefrom using affinity chromatography as taught by Kolch et al. The motivation is provided by Koch et al. who suggest the use of said purified proteins the production of antisera, for example, *supra*. The solution of a protein used for the production of antisera meets the definition of a pharmaceutical composition according to the specification (page 35).

The teachings of Przybyszewska et al. provide the motivation to make a pharmaceutical composition comprising a raf protein to be administered for stimulation of angiogenesis. It would have been obvious to use a human Raf protein or its known active fragments taught by Kolch et al. in said pharmaceutical composition. With regard to claim 41, it is customary to make a pharmaceutical composition comprising at least 0.1 weight percent of an active ingredient.

It would have been further obvious to one of ordinary skill in the art to produce an article of manufacture comprising a pharmaceutical composition comprising Raf protein of SEQ ID NO:2 or its fragments and fusions and an identifying label optionally containing instructions for use.

Statement of intended use in a pharmaceutical composition claim does not distinguish it over the prior art product, i.e. a pharmaceutical composition comprising Raf protein is the same product independent on its intended use.

Response to Arguments

Applicant's arguments filed October 10, 2003 have been fully considered but they are not persuasive.

With regard to the art rejections over Freed et al. and Chow et al., Applicants argue that said references do not "teach or suggest a pharmaceutical composition *consisting essentially of at least about 0.1 weight percent* of the specified active Raf proteins in a physiologically tolerable excipient or carrier, as required by presently amended claim 41" (Remarks, page 5 and page 6). This is not persuasive because as

explained above, the references definitely suggest a pharmaceutical composition that can be just a buffer solution intended for a treatment. With regard to the limitation "*consisting essentially of at least about 0.1 weight percent*", practically any composition meets this limitation because it is an open range concentration. Thus, claim 41 encompasses any concentration starting from 0.1 percent.

The instant claims are drawn to a pharmaceutical composition or an article of manufacture comprising thereof. The product, i.e. human Raf protein (SEQ ID NO:2), is known in the art, Raf-caax of SEQ ID NO:7 is known. Preamble of intended use in a pharmaceutical composition claim in no way distinguishes it over the prior art product. It is the same composition notwithstanding its intended use. It appears that Applicants consider the pending claims equal to method claims but they are not.

With regard to an article of manufacture, it comprises, in addition to a pharmaceutical composition, a label. It appears obvious to label chemical compounds, in the instant case a pharmaceutical composition comprising Raf protein. The examiner's position is that the words on the label are irrelevant since said words and the label itself cannot be patented and cannot impart the patentability to the product. Said words in no way can constitute a substitution for method steps.

Applicants fuerther argue that neither Freed at al. nor Chow et al. "teach or suggest the use of such compositions to stimulate angiogenesis, as set forth in the label limitation of the claim" (Remarks, page 6). It appears that Applicants equal the instant claims with the method claims for treating the condition associated with deficient angiogenesis. However, the current claims are drawn to a product that comprises an

active ingredient, Raf, and a label. Raf is known in the prior art. Applicants argue that "In claim 1, the printed matter on the label should be given patentable weight because the instructions and information on the label impart functionality to the composition. Furthermore, the information on the label vis-à-vis the ability of active Raf proteins to stimulate angiogenesis, is novel, and informs the user of the article how the article is to be utilized. This label limitation is analogous to the situation in Miller where the item at issue was a measuring cup" (page 7). This is not agrred with because in In re Miller, the label was printed on the cup, i.e. the cup itself was changed resulting in a new product while Raf is the same in the prior art and the claims. Applicants further discuss In re Gulack and assert that it "involved a band imprinted with a series of digits derived from a mathematical algorithm. The band could be a hatband, for example, having utility on its own. The printed matter on the band conveyed a new utility to the band, i.e., it was now useful for performing "magic tricks" and for displaying various aspectes of number theory" (page 7). This is not persuasive because the claimed band had a new utility only after the band of the prior art was changed, i.e. the product itself is different from the prior art product. The prior art band, i.e. the band without the imprinted digits is not usable for the same purposes as the claimed band. In Gulack, the printed matter not conveys but imparts a new utility to the band. Contrary to that, in the instant case, Raf is the same prior art protein and the label does not impart any new property or utility to Raf but only conveys the intended use. However, the claims are not drawn to a method of use that may be novel, but to the product.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

February 19, 2004